IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Gleave, et al.	
Application No.: 09/944,326	
Filed: 8/30/2001	Group Art Unit: 1635
Title: TRPM-2 Antisense Therapy	Examiner: Tracy Ann Vivlemore
Attorney Docket No.: UBC.P-020-2	Confirmation No: 2324
Customer No.: 57381	

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

RESPONSE TO OFFICIAL ACTION

Dear Sir:

This is in response to the Office Action mailed March 19, 2007 for the above-captioned application.

The sole issue remaining in this case is the rejection of claims 1, 19 and 30 for obviousness-type double patenting over US Patent No. 6,900,187 in view of US Patent No. 5,877,309 and US Patent No. 5,945,920.

Applicants continue in their position that an obviousness-type double patenting rejection is improper in this case. As a first matter, Applicants again note that MPEP § 804 states the following standard for an obviousness-type double patenting rejection:

> Where the claims of an application are not the "same" as those of a first patent, but the grant of a patent with the claims in the application would **unjustly** extend the rights granted by the first patent, a double patenting rejection under nonstatutory grounds is proper.

In rejecting the claims of this application for obviousness-type double patenting, the Examiner has offered no reasons why any term extension would be unjust **in this case**, nor any reason why it would be a burden on the art to allow separate patents to issue without a requirement for common ownership. The statement of the general rationale for requiring a terminal disclaimer even in 20-year term cases which bridges Pages 7 and 8 of the official action is not a substitute for an explanation of why the rejection should be applied in this case.

As has previously been explained, the published PCT disclosure of the sequence listing (Seq ID No. 4) which is common to both the present claims and the claims of the issued patent occurred more than a year before the filing of the application which led to the '187 patent. The Examiner states that because the PCT application was available as a parent to both applications it is not available as 102(b) art, and therefore that Applicants' arguments about the PCT publication being art are invalid. In response, Applicants point out that the priority claim was made as a continuation-in-part (CIP), and that CIP's are not automatically entitled to the priority claim unless the subject matter claimed was disclosed in the earlier application. Here, the specific modifications of the '187 patent claims were not in the prior application. Further, the Examiner's statement of reasons for allowance mailed January 10, 2005 read: "the claims were interpreted as requiring the sequence with the specified modifications, as such this sequence could not be found in the prior at." Applicants submit that this reliance on the modifications reflects the Examiner's understanding that the specific modifications made the claims of the '187 patent allowable, even over the prior disclosure of the sequence of bases without the specific modifications. Thus, the Examiner did not rely on the common ownership and common inventorship of the two applications in deciding to allow the '187 patent.

Because of this, the rejection in the present case is in error. There is no logical basis for an obviousness-type double patenting rejection in the circumstance where a patent with species claims has issued in a continuation-in-part application, and the full disclosure of the pending parent application was available against those species claims as prior art.

The claims in the later application have been determined to be patentably distinct by an Examiner of the USPTO, based on the content of the claims and not on the common inventorship or ownership of the patent. Thus, the double-patenting rejection as made in the present application places an inventor who improves his own prior work in a worse position than a stranger who made the same improvement. This is inequitable and not what the double-patenting doctrine was intended to achieve.

Furthermore, it places the patent office in the position of putting the validity of the issued patent in doubt because the Examiner now asserts that the issued subject matter is obvious over the present sequence (which was part of the prior art) and some additional references. As explained in the following paragraphs, this argument is in error on the merits. Nevertheless, it is an argument **that should never have been made**, and which never would have been made but for the erroneous rejection for obviousness-type double patenting.

Turning now to the Examiner's egregious attempt to undermine the validity of an issued United States patent, Applicants point out that the claims of the '187 patent are directed to a specific sequence with modifications of a specific types at specific locations. The secondary references cited by the Examiner have nothing to do with this specific sequence, and do not disclose modifications at the specific locations within this sequence. As such, the Examiner has only shows that certain techniques were known, but not that the application of these techniques as reflected in the references would lead to the structures claimed in the '187 patent. The assertion of "mere design choice" is not a substitute for a showing that the result of a design effort would have been obvious.

The possibilities for making modifications to a nucleic acid sequence of 21 bases are essentially endless. In the case of the '187 patent, the claims specifically state that the whole sequence has a phosphorothioate backbone. Furthermore, the claims specify that 4 bases on each end are 2'-O-methoxyethyl modified, and that the cytosines within these end regions are methylated at the 5' position. Published research has shown that changes in the size of the gap effect efficacy of the antisense molecule with locked nucleotides, but it has also shown that at

least in 3rd generation gapmers with locked nucleotides (as opposed to second generation as in the claims of the '187)) this affect can be sequence dependent, with one type of sequence motif in the gap cause an increase in affinity with increasing length of unmodified nucleotides in the middle, and another sequence motif causing a decrease in affinity with increasing gap length. (Exhibit. A, Pages 6367-68) Thus, there is no basis to predict that a gap length of 13 would be desirable or optimal for the particular sequence at issue here. Similarly, the choice of 4 bases at each end for modification is not the only option for the placement of MOE modifications. (See exhibit A, and Exhibit B, page 121 where a single MOE modification and a complete sequence MOE modification are discussed.) Exhibit C, Table 1 shows the boxed bases are 2'-MOE modifications, only one of which (structure 13) is 4 bases at each end. Exhibit D shows other choices on a different nucleotide, and does not argue in favor of any particular structure (other than against structure 6 which has all but one base 2'MOE modified). Thus, the structure as claimed is merely one among many options and there is not suggestion of using the particular structure with this particular sequence.

In view of the foregoing, Applicants submit that even if an obviousness-type double patenting rejection could be properly made in this case, the Examiner has not shown that the issued patent claims are obvious variants of the underlying sequence disclosed and claimed in this application. Thus, Applicants submit that this application is now in form for allowance.

Respectfully submitted,

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